

WE CLAIM:

1. An isolated, water-soluble polypeptide which consists essentially of amino acid residue sequence

SAKGIDYDKL IVRFGSSKID KELINRIERA TGQRPHHFLR RGIFFSHRDM
5 NQVLDAYENK KPFYLYTGRG PSSEAMHVGH LIPFIFTKWL QDVFNVPLVI
QMTDDEKYLW KDLTLDQAYG DAVENAKDII ACGFDINKTF IFSDLDYMGD
SSGFYKNVVK IQKHVTFNQV KGIFGFTDSD CIGKISFPAI QAAPSFSNSF
PQIFRDRTDI QCLIPCAIDQ DPYFRMTRDV APRIGYPKPA LLHSTFFPAL
QGAQTKMSAS DPNSSIPLTD TAKQIKTKVN KHAFFSGGRDT IEEHRQFGGN
10 CDVDVSFMYL TFFLEDDDKL EQIRKDYTSG AMLTGELKKA LIEVLQPLIA
EHQARRKEVT DEIVKEFMTP RKLSFDFQ (SEQ ID NO:12)

or an angiogenesis inhibiting fragment thereof;

said isolated polypeptide having a size of no more than about 45 kilodaltons.

15 2. The isolated polypeptide in accordance with claim 1 which is an angiogenesis inhibiting fragment capable of inhibiting ocular neovascularization.

3. The isolated polypeptide in accordance with claim 1 which is an angiogenesis inhibiting fragment capable of inhibiting ocular
20 neovascularization and which includes at least one of amino acid residue signature sequences HVGH (SEQ ID NO:10) and KMSAS (SEQ ID NO:11).

4. The isolated polypeptide in accordance with claim 1 which is an angiogenesis inhibiting fragment capable of inhibiting ocular
neovascularization and which includes amino acid residue signature sequence
25 HVGH (SEQ ID NO:10).

5. The isolated polypeptide in accordance with claim 1 which is an angiogenesis inhibiting fragment capable of inhibiting ocular neovascularization and having a size of less than about 43 kilodaltons.

6. An isolated polypeptide having the amino acid residue
30 sequence of SEQ ID NO:7.

7. An isolated polynucleotide having a nucleotide sequence at least 95 percent identical to the sequence of a polynucleotide selected from the

group consisting of a polynucleotide of SEQ ID NO:6, a polynucleotide hybridizable to SEQ ID NO:6, a polynucleotide that encodes the polypeptide of SEQ ID NO:7, a polynucleotide that encodes a polypeptide of SEQ ID NO:12, a polynucleotide that encodes a polypeptide epitope of SEQ ID NO:7, and a polynucleotide that is hybridizable to a polynucleotide that encodes a polypeptide epitope of SEQ ID NO:7.

8. A recombinant vector which comprises the isolated nucleic acid molecule of claim 7.

9. A recombinant host cell which includes the vector of claim 8.

10. A recombinant host cell that expresses the polypeptide of claim 1.

11. A method for inhibiting ocular neovascularization in a patient which comprises administering to said patient an ocular neovascularization inhibiting amount of a water-soluble polypeptide consisting essentially of amino acid residue sequence

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QMTDDEKYLW KDLTLDQAYG DAVENAKDII ACGFDINKTF IFSDLDYMG
SSGFYKNVVK IQKHVTFNQV KGIFGFTDSD CIGKISFPAI QAAPSFNSF
PQIFRDRTDI QCLIPCAIDQ DPYFRMTRDV APRIGYPKPA LLHSTFFPAL
QGAQTKMSAS DPNSSIIFLTD TAKQIKTKVN KHA FSGGRDT IEEHRQFGGN
CDVDVSFMYL TFFLEDDDKL EQIRKDYTSG AMLTGELKKA LIEVLQPLIA
EHQARRKEVT DEIVKEFMTP RKLSFDFQ (SEQ ID NO: 12)

or an ocular neovascularization fragment thereof.

12. The method in accordance with claim 11 wherein the administration is effected daily.

13. The method in accordance with claim 11 wherein the administration is effected weekly.

14. The method in accordance with claim 11 wherein the administration is effected monthly.

15. The method in accordance with claim 11 wherein the administration is effected quarterly.

16. The method in accordance with claim 11 wherein the administration is effected semi-annually.

5 17. The method in accordance with claim 11 wherein a polypeptide daily dose of about 20 to about 100 micrograms is administered to the patient.

10 18. The method in accordance with claim 11 wherein a polypeptide quarterly dose of about 2 to about 9 milligrams is administered to the patient.

19. The method in accordance with claim 11 wherein the administration is effected by intravitreal delivery.

20. The method in accordance with claim 11 wherein the administration is effected by intraocular delivery.

15 21. The method in accordance with claim 11 wherein the administration is effected by a sustained delivery device.

22. The method in accordance with claim 11 wherein the administration is effected by gene therapy.

20 23. The method in accordance with claim 11 wherein the administration is effected by cell-based ocular delivery.

24. An injectable angiostatic composition which comprises a polypeptide consisting essentially of amino acid residue sequence

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25 QMTDDEKYLW KDLTLDQAYG DAVENAKDII ACGFDINKTF IFSDLDYMG
SSGFYKNVVK IQKHVTFNQV KGIFGFTDSD CIGKISFPAI QAAPSFNSF
PQIFRDRTDI QCLIPCAIDQ DPYFRMTRDV APRIGYPKPA LLHSTFFPAL
QGAQTKMSAS DPNSSIFLTD TAKQIKTKVN KHA FSGGRDT IEEHRQFGGN
CDVDVSFMYL TFFLEDDDKL EQIRKDYTSG AMLTGELKKA LIEVLQPLIA
30 EHQARRKEVT DEIVKEFMTP RKLSFDFQ (SEQ ID NO: 12)

or an angiogenesis inhibiting fragment thereof, and a pharmacologically acceptable aqueous excipient, the composition containing the polypeptide in a concentration of at least 0.1 milligrams per milliliter of the aqueous excipient.

25. The angiostatic composition in accordance with claim 24 wherein the polypeptide has the amino acid residue sequence of SEQ ID NO:7 or SEQ ID NO:12 and is present at a concentration in the range of about 0.1 to about 0.5 milligrams per milliliter of aqueous excipient.

26. A method of assaying the angiogenesis inhibiting activity of a composition comprising:

a) providing a newborn mouse of less than about 7 days postnatal age;

b) providing a solution of a composition to be assayed;

c) injecting the solution into an eye of the mouse on about day 7 or 8 postnatal;

d) euthanizing the mouse on about day 12 or 13 postnatal and removing the injected eye therefrom;

e) excising the retina from the injected eye and staining the retina with a rabbit anti-mouse collagen IV antibody and a fluorescent-labeled goat anti-rabbit IgG antibody to visualize the vascular network of the retina; and

f) microscopically comparing the degree of vascularization of the deep outer vascular plexus of the retina exposed to the composition to be assayed with the degree of vascularization of a retina from a mouse eye of the same age, and similarly stained, which was not exposed to the composition; wherein a substantially lower level of vascularization in the retina exposed to the composition indicates inhibition of angiogenesis by said composition.

27. A kit for inhibiting ocular neovascularization comprising a quantity of a polypeptide according to claim 1 sufficient for at least a single dosage administration, packaged in a suitable sealed container; at least one self-sealing syringe needle having a gauge of less than about 33, suitable for intravitreal injection; and at least one precisely calibrated syringe.

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